Remarks/Arguments

After entry of this Amendment, claims 25, 26, and 28-38, as amended, will be pending in the application for the Examiner's review and consideration. Claims 1-24 and 27 have been canceled without prejudice. The right to prosecute the subject matter of any of canceled claims 1-24 and 27 in this or in a continuation, continuation-in-part, or divisional application is hereby expressly reserved.

I. Interview Summary

The undersigned appreciates the courtesies extended to her by Examiner Choi in the personal interview held on May 3, 2010. In the Interview, the rejections of the claims under 35 U.S.C. § 103(a) were discussed, and Examiner acknowledged that Applicant's arguments and amendments would appear to overcome the rejections of record. Other topics discussed in the Interview are included in the Remarks that follow.

II. Claim Amendments

Claims 28-30 have been amended to depend from pending claim 25, rather than from canceled claim 1.

Claim 35 has been amended to recite that the composition does not comprise tyrosine, as discussed in the Interview. This Amendment is supported, for example, by paragraph 32 on page 14 of the Specification as filed, which recites the optional inclusion of tyrosine in the composition. "If alternative elements are positively recited in the specification, they may be explicitly excluded in the claims." M.P.E.P. § 2173.05(i).

No new matter has been added to the claims by these amendments.

III. Claim Rejections under 35 U.S.C. § 112

Claims 35-38 stand rejected under 35 U.S.C. § 112, first paragraph as allegedly failing to comply with the written description requirement for the recitation that "the composition does not comprise an amino acid." This rejection has been rendered moot by the amendment of claim 35 to replace "amino acid" with "tyrosine," as discussed in the Interview.

Claims 28-30 stand rejected under 35 U.S.C. § 112, second paragraph as allegedly indefinite for being dependent on canceled claim 1. This rejection has been rendered moot by the amendment of claims 28-30 to depend from pending claim 25, rather than from canceled claim 1.

For these reasons, it is respectfully requested that the Office withdraw the claim rejections under 35 U.S.C. § 112.

IV. Claim Rejections under 35 U.S.C. § 103

Claims 25, 26, and 31-34 stand rejected under 35 U.S.C. § 103(a) as allegedly obvious over U.S. Patent No. 4,938,969 to Schinitsky and Meisner ("Schinitsky & Meisner") in view of U.S. Patent No. 5,804,594 to Murad ("Murad"); U.S. Patent No. 5,902,591 to Herstein ("Herstein") or U.S. Patent No. 5,140,043 to Darr and Pinnell ("Darr"); THE MERCK INDEX, entry 855 (9th ed. 1976) ("Merck Index"); and J.P. Yuan & F. Chen, *J. Agric. Food Chem.*, 46: 5078-82 (1998) ("Yuan").

Claims 28-30 and 35-38 have been rejected under 35 U.S.C. § 112 as described above, but have not been rejected under 35 U.S.C. § 103(a). To the extent that the Office has chosen to delay examining claims 28-30 and 35-38 over the art in view of the § 112 rejections, and in the interest of furthering the Office's policy of compact prosecution, arguments in support of the patentability of claims 28-30 and 35-38 over the art of record are presented below. It is believed that the arguments presented below will obviate any future § 103 rejections of claims 28-30 and 35-38 over the art of record.

A. Claims 25, 26, and 28-30

Claims 25, 26, and 28-30 recite topical compositions comprising: at least 10% (w/v) ascorbic acid; approximately 10% to 25% (w/v) glucosamine; and water, wherein the composition has a pH of about 3.5 to about 4.1; and wherein the composition is prepared by a process comprising: (a) dissolving about 10% to about 50% of the ascorbic acid in water at a temperature of between about 60°C to about 90°C to provide an aqueous ascorbic acid solution of at least 20% (w/v); (b) cooling the aqueous ascorbic acid solution to below about 40°C; (c) combining the aqueous ascorbic acid solution with water, glucosamine, and ascorbic acid to

provide a composition comprising water, approximately 10% to 25% (w/v) glucosamine and at least 10% (w/v) ascorbic acid; and (d) adjusting the pH of the composition to about 3.5 to about 4.1.

1. The references cited by the Office, even when combined, do not teach or suggest all of the recitations of claims 25, 26, and 28-30

   a. "(a) dissolving about 10% to about 50% of the ascorbic acid in water at a temperature of between about 60°C to about 90°C to provide an aqueous ascorbic acid solution of at least 20% (w/v); (b) cooling the aqueous ascorbic acid solution to below about 40°C"

As previously discussed, none of Schinitsky & Meisner, Murad, Herstein, or Darr teaches or suggests a composition comprising ascorbic acid that has been prepared by a process comprising the steps of "(a) dissolving about 10% to about 50% of the ascorbic acid in water at a temperature of between about 60°C to about 90°C to provide an aqueous ascorbic acid solution of at least 20% (w/v)" and "(b) cooling the aqueous ascorbic acid solution to below about 40°C," as recited in claims 25, 26, and 28-30. (*See, e.g.,* Amendment filed December 3, 2009). The Office cites Merck Index and Yuan to provide the missing teaching of these process steps. This is unavailing for at least the following reasons.

Yuan teaches away from exposing ascorbic acid to a temperature of between about 60°C to about 90°C, as recited in the claims, by showing that heating ascorbic acid at 60°C causes the ascorbic acid to degrade. For example, Yuan reports the presence of at least three degradation products after heating a solution of ascorbic acid in aqueous media at 60°C. (Yuan, pp. 5079, 5081-82, Figure 1). The Office has flatly dismissed this argument, stating: "The Yuan et al. reference does not teach away from the claimed invention as Yuan et al. discloses that there is little degradation at 60 degrees compared to 100 degrees Celsius." (Office Action, p. 10). No matter whether Yuan teaches that there is less degradation at 60°C than at 100°C, Yuan teaches degradation at 60°C and, therefore, one of ordinary skill in the art would be motivated by Yuan as a whole to avoid heating at 60°C in order to avoid any degradation of the ascorbic acid.

Further, Merck Index merely discloses the solubility of ascorbic acid in water (80% at 100°C and 40% at 45°C) and does not and would not teach or suggest to the person of ordinary skill in the art a topical composition comprising ascorbic acid, or a method for preparing such a

topical composition that includes steps (a) and (b) above. From the Merck Index, one would expect the solubility to decrease with cooling and thus provides no motivation for heating in the first place.

Therefore, neither Merck Index nor Yuan, when combined with the teachings of Schinitsky & Meisner, Murad, Herstein and/or Darr, teaches or suggests a topical composition of ascorbic acid made by a process including steps (a) and (b) above, as recited in the claims.

b. "wherein the composition has a pH of about 3.5 to about 4.1"

As previously discussed, none of Schinitsky & Meisner, Murad, Merck Index or Yuan teaches or suggests a composition comprising ascorbic acid that has a pH of about 3.5 to about 4.1, as recited in claims 25, 26, and 28-30. (*See, e.g.,* Amendment filed December 3, 2009). The Office cites Herstein or Darr to provide the missing teaching of the recited pH. This is unavailing for at least the following reasons.

The Declaration of Dr. Lorraine Faxon Meisner under 37 C.F.R. § 1.132 submitted on December 3, 2009 ("Meisner Declaration") clearly establishes through several peer-reviewed journal articles that, at the time of the invention, it would have been entirely unexpected that an ascorbic acid composition would be stable enough for use in a topical composition at a pH of about 3.5 to about 4.1. (Meisner Declaration, ¶¶ 11-12). Dr. Meisner's conclusion is supported not only by the Bauernfeind, Hajratwala, and Kassem articles cited in her Declaration, but also by Herstein and Darr, which were cited by the Office.

Herstein and Darr both acknowledge the instability of ascorbic acid compositions at the pH range recited in the claims. For example, Herstein teaches that emulsions of ascorbic acid having a pH within the range of 3.5 to 4.1 are unstable if they lack an organoclay stabilizer: "As can be seen from the data, the physical appearance of the emulsion initially is acceptable and remains acceptable (no breaking of the emulsion) after 25 days. Without the organoclay ingredient, the emulsion would begin to break down after a few days, i.e., 2-3 days." (Herstein, col. 13, ll. 35-41). In addition, Darr stresses the importance of maintaining the pH of an ascorbic acid composition at "no more than about 3 to 3.5, preferably no more than about 2.5" in order to "ensure[] that greater than 82% of the ascorbic acid remains in the protonated, uncharged form," which "removes the ionic repulsion of the two oxygen groups, thus stabilizing the molecule." (Darr, col. 3, ll. 29-30, col. 4, ll. 7-18).

Therefore, neither Herstein nor Darr, when combined with the teachings of Schinitsky & Meisner, Murad, Merck Index and/or Yuan, teaches or suggests the recited compositions having a pH of about 3.5 to about 4.1.

2. The ascorbic acid in the claimed compositions is surprisingly and unexpectedly more stable than native ascorbic acid

Moreover, as discussed in the Interview, Applicant's Specification asserts that ascorbic acid that has been prepared by the process recited in the claims produces a topical composition that is surprisingly and unexpectedly more stable than a topical composition having "native" ascorbic acid:

> As an example, containers having a 1 to 20% (w/v) concentration of a mixture of pretreated ascorbic acid in a 1:1 to 1:10 ratio, together with ascorbic acid formulated under more standard conditions (i.e., dissolved or added in solid form to a formulation at temperatures of about 20 to about 40°C--"native ascorbic acid") were quite stable when shipped and/or stored under adverse conditions, or even when heated. **The stability of such formulations was enhanced in comparison to conventional low pH formulations containing untreated ascorbic acid**, e.g., low pH creams containing 10% (w/v) untreated ascorbic acid. It is postulated that the observed stability of the present compositions is afforded by an equilibrium reaction between ascorbic acid and monhydroascorbic acid that maintains a stable solution of ascorbic acid.

(Specification, page 13, ¶ 30).

For these reasons, the Office has failed to make out a *prima facie* case of obviousness of any of claims 25, 26 or 28-30. Accordingly, the rejections of claims 25 and 26 under 35 U.S.C. § 103 as obvious over Schinitsky & Meisner in view of Murad, Herstein or Darr, Merck Index, and Yuan cannot stand and should be withdrawn. Further, any rejection of claims 28-30 under 35 U.S.C. § 103(a) as obvious over the cited references is obviated.

B. Claims 35-38

Claims 35-38 recite compositions comprising: at least 10% (w/v) ascorbic acid; approximately 10% to 25% (w/v) glucosamine; and water, wherein: the composition has a pH of

about 3.5 to about 4.1; the composition does not comprise tyrosine; and the composition does not comprise a non-toxic zinc salt.

1. The references cited by the Office, even when combined, do not teach or suggest all of the recitations of claims 35-38

a. "the composition does not comprise tyrosine"

As previously discussed, none of Schinitsky & Meisner, Murad, Herstein, Darr, Merck Index or Yuan teaches or suggests an ascorbic acid composition as recited in the claims, that does not comprise tyrosine. (*See, e.g.,* Amendment filed December 3, 2009).

To the contrary, both Schinitsky & Meisner and Murad stress the importance of the inclusion of an amino acid, such as tyrosine. Every composition referred to in Schinitsky & Meisner contains tyrosine as an ingredient. (*See, e.g.,* Schinitsky & Meisner, col. 3, Table 1). In addition, Murad underscores the function of the amino acid (such as tyrosine) by stating that the amino acid is effective to thicken the skin. (*See* Murad, col. 6, ll. 9-33).

b. "the composition does not comprise a non-toxic zinc salt"

As previously discussed, none of Schinitsky & Meisner, Murad, Herstein, Darr, Merck Index or Yuan teaches or suggests am ascorbic acid composition as recited in the claims, that does not comprise a non-toxic zinc salt. (*See, e.g.,* Amendment filed December 3, 2009).

Schinitsky & Meisner states that "an essential ingredient in the present composition is a non-toxic, water soluble zinc salt . . . without zinc sulfate in the present formation, we have found no beneficial effect." (Schinitsky & Meisner, col. 2, ll. 54-56). Elimination of an essential ingredient from the primary reference renders the combination of references used in the rejection improper. In addition, Murad underscores the function of the transition metal compound by stating that the transition metal compound is effective to bind collagen and elastic tissue to rebuild the skin. (*See* Murad, col. 6, ll. 34-52).

c. "the composition has a pH of about 3.5 to about 4.1"

None of the references cited by the Office teaches or suggests a composition comprising ascorbic acid that has a pH of about 3.5 to about 4.1, for the reasons described in Section IV.A.1.b above.

For these reasons, the Office has failed to make out a *prima facie* case of obviousness of any of claims 35-38. Accordingly, any rejection of claims 35-38 under 35 U.S.C. § 103(a) as

obvious over Schinitsky & Meisner in view of Murad, Herstein or Darr, Merck Index, and Yuan is obviated.

C. Claims 31-34

Claims 31-34 recite topical compositions consisting essentially of: at least 10% (w/v) ascorbic acid; approximately 10% to 25% (w/v) glucosamine; and water, wherein the composition has a pH of about 3.5 to about 4.1.

1. The term "consisting essentially of" in claims 31-34 serves to exclude tyrosine and a transition metal compound from the claimed compositions

The term "consisting essentially of" in claims 31-34 limits the scope of claims 31-34 to the recited ingredients and those that do not materially affect the basic and novel characteristic(s) of claimed method, in accordance with M.P.E.P. § 2111.03. In particular, as discussed below and in the Interview, it is submitted that the term "consisting essentially of" in claims 31-34 serves to exclude tyrosine and a non-toxic zinc salt.

The Office states:

> The Applicant's argument that the phrase "consisting essentially of" excludes both amino acids and transition metals does not provide evidence that the inclusion of the same would materially affect the basic and novel characteristics of the claimed invention. The Applicant's own specification indicates that non-toxic zinc salts and sulfur containing amino acids are suitable for use in the claimed invention, i.e., would have the same basic and novel characteristics of topically treating skin. See *In re Herz*, 537 F.2d 549, 551-52, 190 USPQ 461, 463 (CCPA 1976).

(Office Action, p. 8).

It is believed that the tyrosine and non-toxic zinc salt materially affect the basic and novel characteristic(s) of the claimed compositions because they are active ingredients that, if present, would supplement the activity of the claimed compositions when topically applied to a patient. The person of ordinary skill in the art would have recognized these components as active ingredients by recourse, for example, to the Murad reference cited by the Office and discussed above. Murad states that amino acids (such as tyrosine) are effective, for example, to assist in thickening the skin and that transition metal compounds (such as non-toxic zinc salts) are

effective, for example, to bind collagen tissue to rebuild the skin. (Murad, col. 6, ll. 34-52). The present Specification further underscores the functionality of these ingredients, stating that tyrosine acts as a stimulant to protein synthesis and/or precursor to melanin synthesis. (Specification, page 14, ¶ 32). Thus, the present facts differ substantially from those presented in *Herz*, which dealt with the inclusion of a well-known excipient (dispersant), and not an active ingredient.

2. The references cited by the Office, even when combined, do not teach or suggest all of the recitations of claims 31-34

It is respectfully submitted that claims 31-34 are non-obvious over Schinitsky & Meisner in view of Murad, Herstein or Darr, Merck Index, and Yuan for substantially the same reasons as described for claims 35-38 above. Claims 35-38 recite compositions that comprise ascorbic acid, glucosamine, and water, and do not comprise an amino acid or a non-toxic zinc salt. Claims 31-34 likewise exclude an amino acid and a non-toxic zinc salt by virtue of the claim term "consisting essentially of." Claims 31-34, therefore, differ from the disclosures of the cited references for substantially the same reasons as do claims 35-38.

For these reasons, the Office has failed to make out a *prima facie* case of obviousness of any of claims 31-34. Accordingly, the rejections of claims 31-34 under 35 U.S.C. § 103 as obvious over Schinitsky & Meisner in view of Murad, Herstein or Darr, Merck Index, and Yuan cannot stand and should be withdrawn.

V. Conclusion

In view of the foregoing amendments and remarks, it is respectfully submitted that the claims are in condition for allowance. Early and favorable action by the Examiner is earnestly solicited. If any outstanding issues remain, the Examiner is invited to contact the undersigned at (202) 973-8810 to discuss the same.

No fee is believed to be due for the submission of this response. Should any fees be required, please charge all such fees to Wilson Sonsini Goodrich & Rosati Deposit Account No. 23-2415 (36091-701.501).

Respectfully submitted,

Dated: May 17, 2010

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